IN THE SPECIFICATION

Rewrite the paragraph that begins at page 13, line 25 as follows:

--According to a preferred embodiment of the process of the invention, the genetically manipulated cell line is a stable CHO transformant, most preferably a CHO-Messi (ECACC N. 930805200) transformant selected on the basis of a metabolic marker gene. The culture media is preferably a serum-free culture medium, even more preferably a serum- and protein-free defined medium, such as those commercially available. In a preferred embodiment the cell-culture media is CHOM~~aster~~ASTER®

Rewrite the paragraph that begins at page 13, line 25 as follows:

--The cell line is able to grow in suspension in chemically defined media CHOM~~aster~~ASTER® (Ferruccio Messi Cell Culture Technologies, Zürich, Switzerland) without addition of any serum or proteinaceous component. The duplication time of this cell line is such media (complete and selection media) is of about 24 hours. Transfection of *CHO-Messi* cells with pTZA9 was performed according to the method described in Felgner et al., (1987) Proc. Natl. Acad. Sci. USA, 84:7413-7417, and respected the recommendations of the tranfection's reagent manufactureer. Briefly 1µg DNA expression vector pTZA9 (of a solution of 100µg/ml) was mixed with 30µl L~~ipofectin~~IPOFECTIN® (GIBCO® BRL, Life Technologies) in about 500µl exponentially growing *CHO-Messi* cells (about 1 x10^6 cells). The transfection mixture was kept 30min at room temperature, before adding CHOM~~aster~~ASTER® medium supplemented with 25.1mg/l Tryptophan and incubating overnight at 37°C.--

Rewrite the paragraph that begins at page 14, line 12 as follows:

--Stable transfected cells were obtained after limiting dilution in selective CHOM~~aster~~ASTER® medium (without Tryptophan), with the adddition of serine (0.02g/l) and indole (0.35g/l).--

Rewrite the paragraph that begins at page 14, line 15 as follows:

--Selection of the Urokinase producing clones occurred by dilution of the transfection mixture with selective CHOM~~aster~~ASTER® medium in microtiter wells. Another system used for obtaining selected single clones producing Urokinase was to dilute 1:10 a cell suspension of about 10^3 cells/ml with a highly viscous solution of 0.2g/l ~~Methocel~~ETHOCEL® in selective CHOM~~aster~~ASTER® medium with addition of 4% dialysed fetal calf serum onto a 24-well cluster plate and after 2 weeks single clones were picked up with a sterile pipette tip and a new culture in suspension was started.--

Rewrite the paragraph that begins at page 14, line 23 as follows:

--The following culture strategy was adopted for the preparation of the inoculum in the bioreactor. A cell culture raised in microtiter wells was further split 1:3 with selective CHOM~~aster~~ASTER® medium in larger wells (24-well cluster and 6-well cluster plates) and subsequently in 5- and $75cm^2$-T flasks once the cell density reached about 4-5 x 10^5 cells/ml.--

Rewrite the paragraph that begins at page 15, line 8 as follows:

--In table 1 are reported the cell viability and the *uPA* yield after 5 days cultivation in 1L Spinner-flask culture at 37°C and at different Na-butyrate concentrations. *uPA* activity was followed by a chromogenic assay using the ~~P~~efachrome<u>EFACHROME®</u> UK(54-46) (Pentapharm. LTD, Basel, Switzerland) as chromogenic substrate, according to the manufacturer's instructions; the cell viability was followed every day and measured microscopically after Trypan blue dye-exclusion method, as described in Doyle et al. A, Griffiths, JB and Newell, DG (Eds.) (1994), in "Cell & Tissue Culture: Laboratory Procedures". John Wiley & Sons. New York.--

Rewrite the paragraph that begins at page 17, line 7 as follows:

When the cellular density reached values of about 2 x 10^6 living cells/ml, the cells were separated from the exhausted medium by tangential filtration (or centrifugation). Cells were then resuspended in the bioreactor in the same original volume of fresh medium CHOM~~aster~~<u>ASTER®</u> with the addition of sodium butyrate to achieve a final concentration of 1.2mM.--

Rewrite the paragraph that begins at page 17, line 17 as follows:

--The production of active u-PA (*tc-uPA HMW* and *LMW*) was monitored by a chromogenic test on a specific substrate, ~~P~~efachrome<u>EFACHROME®</u> UK. A progressive increase of the activity was observed up to maximal values as high as 7000 IU/ml, achieved after 4-5 days of fermentation. At this point the cells were harvested and subsequently discarded and the exhausted culture medium, containing *tc-uPA*, was further processed for purification.

Rewrite the paragraph that begins at page 18, line 22 as follows:

--The supernatant of the cell culture grown in bioreactor, obtained as described in Example 3 was acidified by addition of CH_3COOH to a pH of 54.5 and cleared from cellular debris by filtration on 0.45µm filter. T~~ween~~WEEN®-80 0.01% was added and the supernatant was loaded onto an ion exchange chromatography column (SP S~~epharose~~EPHAROSE® Big Beads, Amersham-Pharmacia) previously equilibrated with a 20mM pH 6.0 sodium phosphate buffer solution. The column bed size was 10cm height, 2.6cm diameter. The flow rate during loading and washing was 10ml/min and during elution was 2ml/min.--

Rewrite the paragraph that begins at page 19, line 15 as follows:

--The eluate obtained, containing Urokinase (tc-uPA HMW) was brought to pH6.5 by the addition of 1N NaOH. Then it was loaded on to a benzamidine S~~epharose~~EPHAROSE® 6B affinity column, previously equilibrated with at least 2 volumes of a 20mM sodium phosphate, 400mM NaCl, pH 6.5 buffer solution.--

Rewrite the paragraph that begins at page 20, line 27 as follows:

--Characterization of recombinant *tc-uPA HMW* was carried out in comparative studies with the commercial extractive *tc-uPA HMW* (UKIDAN~~kidan~~®, Serono) by mass spectroscopy and functional studies.--